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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,267	WONG, GRACE	
	Examiner	Art Unit	
	Catherine S. Hibbert	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *13-16,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 17-19* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 June 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :21 June 2004, 29 July 2004, and 15 February 2006.

DETAILED ACTION

This is the First Office action on the Merits of the application filed on 21 June 2004, which claims benefit of the International Filing Date on 19 December 2002, which claims benefit of the Provisional Application No. 60/344,293 filed 21 December 2001. The Applicant's response to restriction requirements filed on 25 January 2007 is acknowledged. Claims 1-21 are pending. Claims 13-16 and 20-21 are drawn to non-elected inventions/species and are withdrawn. Claims 1-12 and 17-19 are under examination.

Election/Restrictions

Claims 13-16 and 20-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 25 January 2007.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see specification p. 1, ¶2, line 11 and p. 2, ¶3, line 2).

Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The disclosure is objected to because of the following informalities: the following typographical errors/word omissions were found in the specification "transcript" on page 2, ¶4, line 2, should be --transcripts--, "does directly" on page 2, ¶5, line 5 should read --does not directly--, and "identification sparsely" on page 3, ¶7, line 7 should read --identification of sparsely--.

Appropriate correction is required.

Claim Objections

Claim 1 is objected to because of the following informalities: Claim 1 contains two (c) steps. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 and 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim

term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "exposing" in claim 1 is used by the claim to hold two reasonable interpretations in light of the applicant's list of "stimulatory factors" listed in the dependent claim 9. For example, the list of "stimulatory factors" in claim 9 includes factors that one could "expose" cells to, such as "a hormone", which represents the accepted meaning of "exposing" as meaning "applied to from the outside", but also includes in the list of "stimulatory factors", the term "genetic defect", which suggests an alternative interpretation of the term "exposing" to mean "choosing a cell source that "contains" a "genetic defect" or perhaps "choosing a cell source that is in a diseased state due to a genetic defect. The term is indefinite because the specification does not clearly redefine the term. The claims 2-12 and 17-19 are indefinite insofar as they depend from claim 1.

Claims 6 and 10 recite the limitation "the cell source" in the first line of the claims. There is insufficient antecedent basis for this limitation in these claims. Claims 6 and 10 depend from claim 1. However, claim 1 recites "a first cell source" in step (a) and recites "a second cell source" in step (d) and therefore it is unclear whether the term "the cell source" in claims 6 and 10 refers to the first or second cell source (or both) from claim 1. Claims 7 and 11 and 12 are also indefinite insofar as they depend from claims 6 and 10.

Claim 7 recites the limitation "wherein the reproductive cell" in line 1. There is insufficient antecedent basis for this limitation in the claim because the claim, as written,

depends from claim 3 where there is no antecedent basis for "the reproductive cell". It appears that claim 7 contains a typographical error and is meant to depend from claim 6 where there is clear antecedent basis for "the reproductive cell". Therefore, in the interest of compact prosecution, claim 7 will be examined as if it depends from claim 6 instead of from claim 3.

35 U.S.C. 112 (1st)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. In claim 1, a step that would result in a signal which is indicative of "an expressed protein", critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Claim 1 recites the limitation "wherein increased signal from the stimulated source indicates an expressed protein" in step (e). However, there is nothing in the method steps (a)-(e) of claim 1 that would result in a signal which is indicative of "an expressed protein" rather than an expressed RNA. The method is not enabled because the method detects the expressed RNA and not all RNA is translated into expressed proteins. For example, certain RNA molecules function as catalytic subunits for ribozymes ("Ribozymes Come Ready for Action, HHMI News: 9 October 1998). The omitted step is considered an essential step of claim 1 because Applicant states in line 1 that claim 1 is "A method of identifying a protein". Claims 2-12 and 17-19 rejected insofar as they depend from claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 3, 5, 9 and 18 are rejected under 35 U.S.C. 102(b) as anticipated by Zanders *et al.* (Zanders *et al.*, "Analysis of immune system gene expression in small rheumatoid arthritis biopsies using a combination of subtractive hybridization and high-density cDNA array" in *Journal of Immunological Methods*, Vol. 233, 13 January 2000, pp. 131-140).

Claim 1 is directed to a method of identifying a protein expressed in response to a stimulatory factor comprising the steps of: (a) exposing a first cell source to one or more stimulatory factors, (b) creating a first library of nucleic acids isolated from the stimulated first source, (c) creating a second library of nucleic acids from the first cell source not exposed to the stimulatory factors, "(c)" creating an array of nucleic acids by subjecting the first and second library to subtractive hybridization and creating an array of remaining nucleic acids, (d) taking a second cell source and exposing the second source to one or more stimulatory factors and isolating nucleic acids from the second source with and without stimulation, and (e) hybridizing the nucleic acids from the second source with and without stimulation to the array, wherein increased signal from the stimulated source indicates an expressed protein.

Zanders *et al.* teaches the method of claim 1 comprising creating a first and second library of nucleic acids isolated from a cell source which has (or has not) been exposed to a "stimulatory factor" and creating an array of nucleic acids by subjecting the first and second library to subtractive hybridization and creating an array of the remaining nucleic acids. For example, Zanders *et al.* isolated total RNA from synovial tissue from patients "exposed" to rheumatoid arthritis and from synovial tissue from normal control human subjects without rheumatoid arthritis (abstract lines 1-2 and p. 133, lines 7-13), and created full-length cDNA libraries from the RNA (abstract line 5 and p. 133, lines 7-13, and Fig. 1), and created a nucleic acid array by subjecting the first and second libraries to subtractive hybridization (see p.133, section 2.3 "PCR suppression subtractive hybridization), and creating a nucleic acid array with the subtracted library (p.134, Section 3.2, lines1-6 and Fig.2).

Zanders *et al.* further teaches the method steps (d) and (e) of claim 1 comprising isolating nucleic acids from a second source (with and without stimulation), and then hybridizing the nucleic acids from the second source (with and without stimulation) to the array, wherein increased signal from the stimulated source indicates an expressed protein (Fig.2). For example, Zanders *et al.* recites "the cDNA obtained after subtractive hybridization was used to screen two high-density arrays of clones picked from the RA-Nor library, as well as those from the I.M.A.G.E consortium" (p.134, Section 3.2, lines1-6 and Fig.2). Applicant indicates in the instant specification that the "second source", used for the hybridization against the array "may be the same as used for the creation of the libraries but it may also be a different source" (see instant specification ¶29, lines 3-4). Therefore, Zanders *et.al.* anticipates all of the limitations of claim 1.

Claim 2 is directed to the method of claim 1 and further comprising a step of picking a clone corresponding to the increased signal from the first library and sequencing the clone. Zanders *et al.* teaches the method of claim 1 (above) and further teaches a step of picking a clone corresponding to the increased signal from the first library and sequencing the clone, "clones displaying strong/medium hybridization to RA-Nor probes (but not Nor-RNA) are identified by sequence analysis" (see Figure legend 2C). Therefore, Zanders *et al.* anticipates all of the limitations of claim 2.

Claim 3 is directed to the method of claim 2 and further comprising a step of subjecting the sequence of the clone to a sequence comparison software wherein a sequence that has less than about 50% homology with known sequences is a novel sequence. Zanders *et al.* teaches the method of claim 2 (above) and further teaches subjecting the sequence of the clone to the BLAST sequence comparison software (p. 134, Section 2.7 lines 1-8 and Section 3.3 lines 1-7). Zanders *et al.* further recites "A number of sequences had no database match, thus providing a source of novel gene fragments for further analysis" (p. 134/135, Section 3.3 lines 12/1-2). Therefore, Zanders *et al.* anticipates all of the limitations of claim 3.

Claim 5 is directed to the method of claim 1, and further comprising wherein the nucleic acid is RNA or cDNA. Zanders *et al.* teaches the method of claim 1 (above) and further teaches wherein the nucleic acid is RNA or cDNA. For example, Zanders *et al.* created full-length cDNA libraries from the isolated total RNA from tissue extraction (abstract line 5 and p. 133, lines 8-13, and Fig. 1). Therefore, Zanders *et al.* anticipates all of the limitations of claim 5.

Claim 9 is directed to the method of claim 1 and further comprising wherein the stimulatory factor is selected from a group comprising a pathogen, genetic defect, radiation, heat,

a hormone, a growth factor, a cytokine, or mixture thereof. Zanders *et al.* teaches the method of claim 1 (above) and further teaches wherein the stimulatory factor is a cytokine resulting in rheumatoid arthritis (abstract, line 2). Therefore, Zanders *et al.* anticipates all of the limitations of claim 9.

Claim 18 is directed to the method of claim 1 and further comprising wherein the exposure of step (a) is performed *in vivo*. Zanders *et al.* teaches the method of claim 1 (above) and further teaches wherein the "exposure" step is performed *in vivo*. Zanders *et al.* recites "synovial tissue was obtained from patients with RA" or directly from human subjects without RA (p. 132, Section 2.1, lines1-5). Therefore, Zanders *et al.* anticipates all of the limitations of claim 18.

35 USC § 102

Claims 1, 6-7 and 10-12 are rejected under 35 U.S.C. 102(a) as anticipated by Robert *et al.* (Robert, C. *et al.*, "Differential Display and Suppressive Subtractive Hybridization Used to Identify Granulosa Cell Messenger RNA Associated with Bovine Oocyte Developmental Competence" in Biology of Reproduction 64, p. 1812-1820, p.d. June 1, 2001.)

Claim 1 is directed to the method described above.

Robert *et al.* teaches the method of claim 1 comprising creating a first and second library of nucleic acids isolated from a cell source which has (or has not) been exposed to a "stimulatory factor" and creating an array of nucleic acids by subjecting the first and second library to subtractive hybridization and creating an array of the remaining nucleic acids. For example, Robert *et al.* isolated total RNA from granulosa cells "cultured in the presence or absence of LH" (abstract, lines 8-10 and p.1813, ¶ 2, lines1-2) and created full-length cDNA libraries from the

RNA (p. 1814, ¶ 5, lines 1-7), and created a nucleic acid array by subjecting the first and second libraries to subtractive hybridization (see p.1814, ¶ 6, lines 1-2), and creating a nucleic acid array with the subtracted library. (p.1814, ¶ 9, lines 1-4 and 20-24 and Fig. 2).

Robert *et al.* further teaches the method steps (d) and (e) of claim 1 comprising isolating nucleic acids from a second source (with and without stimulation), and then hybridizing the nucleic acids from the second source (with and without stimulation) to the array, wherein increased signal from the stimulated source indicates an expressed protein (Fig.2). For example, Robert *et al.* recites: "For SSH clones, the forward and reverse subtraction PCR products were used as probes to hybridize one of each identical dot blot membrane containing the PCR-amplified cDNA inserts." (p. 1814, ¶ 9, lines 20-23 and Fig.2). Applicant indicates in the instant specification that the "second source", used for the hybridization against the array "may be the same as used for the creation of the libraries but it may also be a different source" (see instant specification ¶29, lines 3-4). Therefore, Robert *et al.* anticipates all of the limitations of claim 1.

Claims 6-7 and 10-12 are directed to the method of claim 1, and further comprising wherein the cell source is either a reproductive cell (claim 6), an organ or mixture of organs (claim 10), a reproductive organ (claim 11), an ovary (claim 12), or an ovarian cell (claim 7). Claim 7 is being examined "as directed to the method of claim 6" instead of to claim 3 (see 112 2nd above). Therefore, a method directed to the method of claim 1 and further comprising wherein the cell source is an ovarian cell (from an ovary) reads on all of the limitations of claims 6-7 and 10-12. Robert *et al.* teaches the method of claim 1 (above) and further teaches the cell

source is granulosa cells from "bovine ovaries" (p. 1813, ¶ 2, lines 1-2). Therefore, Robert *et al.* anticipates all of the limitations of claims 6-7 and 10-12.

Claim 8 is directed to the method of claim 1 and further comprising wherein the stimulatory factor comprises one or more compounds selected from a group consisting of FSH, LH, TNF, IFNγ, PMA, LPS, cycloheximide and Indomethacin. Robert *et al.* teaches the method of claim 1 (above) and further teaches wherein the stimulatory factor is LH (i.e. granulosa cells "cultured in the presence or absence of LH were compared" (abstract, lines 8-10). Therefore, Robert *et al.* anticipates all of the limitations of claim 8.

Claim 17 is directed to the method of claims 1 and further comprising wherein the exposure of step (a) is performed *in vitro*. Robert *et al.* teaches the method of claim 1 (above) and further teaches wherein the exposure of step (a) is performed *in vitro* (i.e. granulosa cells "cultured in the presence or absence of LH were compared" (abstract, lines 8-10). Therefore, Robert *et al.* anticipates all of the limitations of claim 8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zanders *et al.* (*supra*). Claim 4 is directed to the method of claim 3 and further comprising a step of expressing the novel sequences. Zanders *et al.* teaches all of the limitations of claim 3 (above) and further contemplates a step of expressing the novel sequences.

It would have been obvious and one would have been motivated to express the novel sequences because Zanders *et al.* recites "it will be necessary to fully characterize those cDNAs without database matches by full-length cloning and expression as a prelude to functional

analysis" (p. 139, ¶ 4, lines 14-20). Therefore, Zanders *et al.* anticipates all of the limitations of claim 4.

Claims 1, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee *et al.* (Lee, K-F *et al.*, "Suppression Subtractive Hybridization Identifies Genes Expressed in Oviduct during Mouse Preimplantation Period", in *Biochemical and Biophysical Research Communications*, Vol. 277, (2000) pp. 680-685) in view of Zanders *et al.* (above).

Claim 1 is directed to the method described above.

Lee *et al.* teaches the method of claim 1 comprising creating a first and second library of nucleic acids isolated from a cell source which has (or has not) been exposed to a stimulatory factor, (PMSG and hCG), and creating an array of nucleic acids by subjecting the first and second library to subtractive hybridization and creating an array of the remaining nucleic acids. For example, Lee *et al.* teaches "MF1 female mice were injected (i.p.) with 5 IU pregnant mare's serum gonadotrophin" (PMSG) and 48 hours later, were injected with 5 IU of human chorionic gonadotrophin (hCG) (p.681, ¶ 3, lines 1-4). Lee *et al.* further teaches creating full-length cDNA libraries from the RNA and nucleic acid arrays by subjecting the first and second libraries to subtractive hybridization (see p.681, ¶ 5, lines 1-15), and creating a nucleic acid array with the subtracted library (p.681, ¶ 10, lines 10-25 and Fig. 1).

Lee *et al.* further teaches the method steps (d) and (e) of claim 1 comprising isolating nucleic acids from a second source (with and without stimulation), and then hybridizing the nucleic acids from the second source (with and without stimulation) to the array, wherein increased signal from the stimulated source indicates an expressed protein (p.681, ¶ 10, lines 10-

25 and Fig. 1). For example, Lee *et al.* recites the subtracted library of clones were amplified by PCR and the PCR products were "dotted onto Hybond N+ membranes" and further teaches the "nonsubtracted cDNA probes from testers and drivers were 32P-labeled using PCR-select Subtraction Hybridization Screening kit" (p.681, ¶ 10, lines 10-25).

Claim 18 is directed to the method of claim 1 and further directed to wherein the exposure of step (a) is performed *in vivo*. Claim 19 is directed to the method of claim 18 and further comprising wherein the *in vivo* exposure is intraperitoneal. Lee *et al.* teaches "MF1 female mice were injected (i.p.) with 5 IU pregnant mare's serum gonadotrophin" (PMSG) and 48 hours later, were injected with 5 IU of human chorionic gonadotrophin (hCG) (p.681, ¶ 3, lines 1-4).

Lee *et al.* differs from the invention claimed in the instant claim 1 in that while it teaches the use of RNA isolated from stimulated versus unstimulated cells for subsequent cDNA subtractive hybridization for preparation of stimulated versus normal cDNA libraries, Lee *et al.* fails to teach that the tester and driver cDNAs for subtractive hybridization are from the same cell source.

Zanders *et al.* teaches the method of making subtractive hybridization cDNA libraries from stimulated versus unstimulated cells using the same cell source (see above).

One would have been motivated at the time the invention was made and it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the same cell source for both the driver and tester cDNAs for the subtractive hybridization in the method taught in Lee *et al.* because Zanders *et al.* teaches that their "subtractive library approach can enrich for genes which are known to be present in chronic inflammation, for example"

(p.132, ¶2, lines 17-20). In addition, Zanders *et al.* teaches their subtractive hybridization method combined with the array analysis had other benefits. Zanders *et al.* recites: "A significant number of sequences were also obtained which had no clear database match, which illustrates the utility of the approach for identifying new gene products expressed in the disease synovium" or in "tissues from other diseases" (p.132, ¶2, lines 25-31). Both Lee *et al.* and Zanders *et al.* are in the same field of endeavor which involves the study of gene expression using subtractive hybridization combined with nucleic acid array methods. Both are directed to the same problem sought to be solved, that of identifying novel genes expressed in cells in response to stimulatory factors.

Absent evidence to the contrary, one would have a reasonable expectation of success combining the teachings of the art because the use of the same cell source for stimulated versus non-stimulated control cells for the purpose of differential gene expression/subtractive hybridization was routinely practiced at the time the teachings of Lee ref *et al.*, and Zanders *et al.* were published.

In view of the foregoing, the methods of claims 1 and 18-19, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC *§103(a)*.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Catherine S. Hibbert whose telephone number is 571-270-3053. The examiner can normally be reached on Monday-Friday, 7:30 AM-5:00 PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Patent Examiner: Catherine S. Hibbert

MARY MOSHER
SUPERVISORY PATENT EXAMINER

4-2-07